Claims

1. A method for the diagnosis of a neonatal or infantile epilepsy syndrome as BFNIS in a patient with seizure onset in the first year of life, comprising testing for the presence of an alteration in the SCN2A gene, including in a regulatory region of the gene, in a patient sample, and establishing a diagnosis which will indicate a high probability of BFNIS when an SCN2A alteration is detected or establishing a diagnosis which will indicate a low probability of BFNIS when an SCN2A alteration is not detected.

2. A method as claimed in claim 1 wherein a diagnosis which will indicate a very high probability of BFNIS is established where the SCN2A alteration is known to be BFNIS associated.

3. A method as claimed in claim 1 wherein a diagnosis which will indicate a very high probability of BFNIS is established where the SCN2A alteration is present in the affected parent or relatives of the patient.

4. A method as claimed in claim 1 wherein a diagnosis which will indicate a very high probability of BFNIS is established where the SCN2A alteration is a missense mutation.

5. A method as claimed in any one of claims 1 to 4 comprising performing one or more assays to test for the presence of an SCN2A alteration and to identify the nature of the alteration.

6. A method as claimed in any one of claims 1 to 4 comprising:

(1) performing one or more assays to test for the presence of an alteration in the SCN2A gene of

the patient; and, if the results indicate the presence of an alteration in the SCN2A gene,

(2) performing one or more assays to identify the nature of the SCN2A alteration.

7. A method as claimed in any one of claims 1 to 6 further comprising testing for the presence of an alteration in the KCNQ2 and/or KCNQ3 genes, including in the regulatory regions of the genes, in a patient sample, and establishing a diagnosis which will indicate a high probability of BFNS when a KCNQ2 or KCNQ3 alteration is detected or establishing a diagnosis which will indicate a likelihood of BFIS when a KCNQ2 or KCNQ3 alteration is not detected.

8. A method for the diagnosis of a neonatal or infantile epilepsy syndrome as one of BFNIS, BFNS or BFIS in a patient with seizure onset in the first year of life comprising:

(1) (a) testing for the presence of an alteration in the SCN2A gene, including in a regulatory region of the gene, in a patient sample; and/or

(b) testing for the presence of an alteration in the KCNQ2 and/or KCNQ3 genes, including in regulatory regions of the genes, in the patient sample; and

(2) (a) establishing a diagnosis which will indicate a high probability of BFNIS when an SCN2A alteration is detected;

(b) establishing a diagnosis which will indicate a high probability of BFNS when a KCNQ2 or KCNQ3 alteration is detected; or

(c) establishing a diagnosis which will indicate a likelihood of BFIS when an SCN2A, KCNQ2 or KCNQ3 alteration is not detected.

9. A method as claimed in claim 8 comprising performing one or more assays to test for the presence of an SCN2A, KCNQ2 and/or KCNQ3 alteration and to identify the nature of the alteration.

10. A method as claimed in claim 8 comprising:

(1) performing one or more assays to test for the presence of an alteration in the SCN2A, KCNQ2 and/or KCNQ3 genes of the patient; and, if the results indicate the presence of an alteration in any one of these genes,

(2) performing one or more assays to identify the nature of the alteration.

11. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is a DNA hybridisation assay.

12. A method as claimed in claim 11 wherein an SCN2A, KCNQ2 or KCNQ3 gene probe, an SCN2A, KCNQ2 or KCNQ3 exon-specific probe, or an SCN2A, KCNQ2 or KCNQ3 allele specific probe is hybridised to genomic DNA isolated from said patient.

13. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is high performance liquid chromatography.

14. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is an electrophoretic assay.

15. A method as claimed in any one of claims 4, 5, 9 or 10 wherein the sample DNA to be tested is quantitatively

amplified for at least one exon of the SCN2A, KCNQ2 or KCNQ3 genes to produce amplified fragments and the length of the amplification products for each amplified exon is compared to the length of the amplification products obtained when a wild-type SCN2A, KCNQ2 or KCNQ3 gene is amplified using the same primers, whereby differences in length between an amplified sample exon and the corresponding amplified wild-type exon reflect the occurrence of a truncating alteration in the sample SCN2A, KCNQ2 or KCNQ3 gene.

16. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays incorporates DNA amplification using SCN2A, KCNQ2 or KCNQ3 allele specific oligonucleotides.

17. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is SSCP analysis.

18. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is RNase protection.

19. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is DGGE.

20. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is an enzymatic assay.

21. A method as claimed in claim 20 wherein said assay incorporates the use of MutS.

22. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays examines the electrophoretic mobility of the SCN2A, KCNQ2 or KCNQ3 proteins of the patient.

23. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is an immunoassay.

24. A method as claimed in any one of claims 4, 5, 9 or 10 wherein one of the assays is DNA sequencing.

25. A method for testing patients for BFNIS-associated mutations in the SCN2A gene comprising the steps of:

a) quantitatively amplifying at least one exon of the SCN2A gene from a body sample of each patient to produce amplified fragments;

b) comparing the properties of the amplified fragments to standard values based upon the fragments produced by amplification of the same exon in a non-mutant SCN2A gene; and

c) determining the nucleic acid sequence of each exon identified in b) that has different properties in the patient compared to the corresponding non-mutant SCN2A exon.

26. A method for testing patients for BFNIS-associated mutations in the SCN2A gene comprising the steps of:

a) quantitatively amplifying, from a body sample of each patient at least one exon of the SCN2A gene using primers complementary to intron regions flanking each amplified exon;

b) comparing the length of the amplification products for each amplified exon to the length of the amplification products obtained when a wild-type SCN2A gene is amplified using the same primers, whereby differences in length between an amplified sample exon and the corresponding amplified wild-type exon reflect the occurrence of a truncating mutation in the sample SCN2A gene; and

c) determining the nucleic acid sequence of each exon identified in b) to contain a truncating mutation.

27. A method for testing patients for BFNIS-associated mutations in the SCN2A gene comprising the steps of:

a) quantitatively amplifying, from a body sample of each patient at least one exon of the SCN2A gene using primers complementary to intron regions flanking each amplified exon;

b) hybridising the fragments from a) with fragments produced by amplification of the same exon in a non-mutant SCN2A gene;

c) determining the nucleic acid sequence of each patient exon identified in b) that either does not hybridise to corresponding wild-type fragments or forms a mismatched heteroduplex.